

## 长序虎皮楠果实中的一个新的生物碱<sup>\*</sup>

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**摘要:** 从长序虎皮楠 (*Daphniphyllum longeracemosum*) 果实的甲醇提取物中分离得到一个新的虎皮楠生物碱和三个已知的环烯醚萜苷型虎皮楠生物碱。通过现代波谱解析技术鉴定为 daphlongeranine F (**1**), caldaphnidine F (**2**), daphcalycinosidine B (**3**) and daphcalycinosidine C (**4**)。其中, 三个环烯醚萜苷虎皮楠生物碱系首次从该种分离得到。

**关键词:** 长序虎皮楠; 虎皮楠生物碱; 环烯醚萜苷型生物碱

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## A New Alkaloid from the Fruits of *Daphniphyllum longeracemosum* (Daphniphyllaceae)

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**Abstract:** A new *Daphniphyllum* alkaloid daphlongeranine F (**1**) along with three known iridoid alkaloids were isolated from the fruits of *Daphniphyllum longeracemosum*. Their structures were determined by spectroscopic analysis including mass spectrometry and 2D NMR. It may be worthy to point out that the three known iridoid alkaloids caldaphnidine F (**2**), daphcalycinosidine B (**3**) and daphcalycinosidine C (**4**) which were rarely distributed in this genus, were obtained from *Daphniphyllum longeracemosum* for the first time.

**Key words:** *Daphniphyllum longeracemosum*; *Daphniphyllum* alkaloid; Iridoid alkaloid

The *Daphniphyllum* genus is remarkable for metabolizing structurally diverse, complex alkaloids with unique polycyclic skeletons (Kobayashi and Morita, 2003). *Daphniphyllum* alkaloids have been challenging subjects in synthetic as well as biosynthetic research fields (Kobayashi and Morita, 2003). The *Daphniphyllum longeracemosum* is an evergreen tree distributed in Yunnan Province, China (Li et al., 2006). Our previous studies on this plant

have resulted in the isolation of a series of novel alkaloids. As further investigation on the fruits of *Daphniphyllum longeracemosum*, a new *Daphniphyllum* alkaloid daphlongeranine F (**1**), together with three known iridoid alkaloids caldaphnidine F (**2**), daphcalycinosidine B (**3**) and daphcalycinosidine C (**4**), were isolated. Herein, we describe the isolation and structure elucidation of daphlongeranine F (**1**) (Fig. 1).

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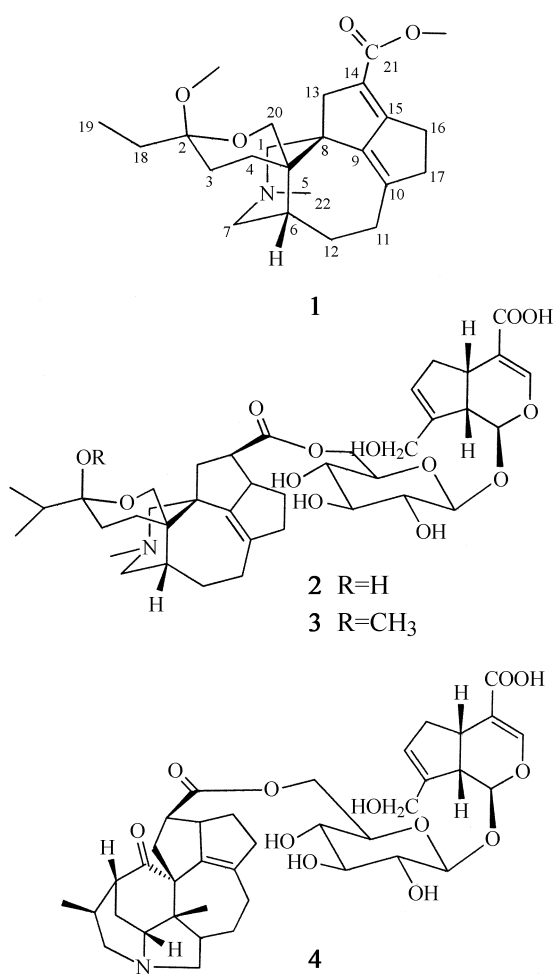
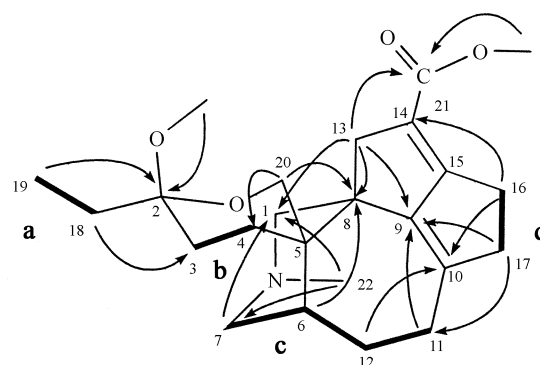


Fig. 1 The structures of compounds 1–4

## Results and Discussion

Daphlongeranine F (**1**) was isolated as an optically active colorless solid and its molecular formula was established as  $C_{24}H_{35}O_4$  on the basis of the positive HRESIMS at  $m/z$  402.2641  $[M+H]^+$ . The UV absorption at 296 nm ( $\log \epsilon = 4.12$ ) and IR bands at  $1692\text{ cm}^{-1}$ ,  $1650\text{ cm}^{-1}$  and  $1620\text{ cm}^{-1}$  indicated the presence of an ester  $C=O$  group conjugated with two  $C=C$  bonds (Chen *et al.*, 2005). The NMR data of **1** displayed the characteristic features of a yuzurine-type *Daphniphyllum* alkaloid, as judged from the presence of an oxygenated methylene ( $\delta_C$  63.1,  $\delta_H$  3.54, dd,  $J = 12.0, 3.1$  Hz and  $\delta_H$  4.13, d,  $J = 12.0$  Hz), a N-methyl ( $\delta_C$  46.1,  $\delta_H$  2.13, br. s) and a quaternary carbon ( $\delta_C$

100.1). Extensive comparison of molecular weight and  $^{13}\text{C}$  NMR of **1** with those of daphgraciline (Yamamura *et al.*, 1980) revealed that they shared highly similar structure, except for the downfield shift of ca. 4 ppm for the quaternary hemiketal carbon ( $\delta_C$  96.0, C-2). It implied that a MeO ( $\delta_H$  3.16) group instead of a OH group was linked to C-2. The structure of **1** was finally established by detailed 2D NMR studies. The  $^1\text{H}, ^1\text{H}$ -COSY correlation signals disclose four substructures: **a** (C-19 to C-18), **b** (C-3 to C-4), **c** (C-6 to C-7, C-6 to C-12 and C-11 to C-12) and **d** (C-17 to C-16) as shown in Fig. 2. The HMBC correlation between the methoxyl protons ( $\delta_H$  3.16) and C-2 ( $\delta_C$  100.1) further confirmed the above speculation. Thus, it allowed the assignment of compound **1** to daphlongeranine F, a new *Daphniphyllum* alkaloid of the yuzurine-type.

Fig. 2 COSY (—) and selected HMBC (---) correlations of Daphlongeranine F (**1**)

The known alkaloids caldaphnidine F (**2**), daphcalycinosidine B (**3**) and daphcalycinosidine C (**4**), the rare iridoid alkaloids, were identified on the basis of reported physical NMR and ES-IMS data. These three iridoid alkaloids were obtained from *Daphniphyllum longeracemosum* for the first time, which were different from ones isolated by our group previously.

## Experimental

**General Experimental Procedures** Optical rotations were measured on a JASCO DIP-370 digital polarimeter.

IR spectra was obtained with a Tensor 27 FT-IR spectrometer with KBr pellets. UV spectra was measured in a UV 210A spectrometer. NMR spectra were recorded on Bruker AM-400 and DRX-500 spectrometers with TMS as internal standard. ESIMS was recorded on a finnigan MAT 90 instrument, HRESIMS spectra on a VG Auto Spec-3000 spectrometer. Column chromatography was performed on silica gel (200–300 mesh; Qingdao Marine Chemical Inc., Qingdao, People's Republic of China), Sephadex LH-20 (40–70  $\mu\text{m}$ , Amersham Pharmacia Biotech AB, Uppsala, Sweden), and Lichroprep RP-18 gel (40–63  $\mu\text{m}$ , Merck Darmstadt, Germany). Fractions were monitored by TLC and spots were visualized by Dragendorff's reagent. HPLC separations were performed using an Agilent 1100 series pump equipped with a UV detector and a Zorbax SB-C18 (10  $\mu\text{m}$ , Agilent Co. Ltd. Wilmington, DE) column (i. d.  $9.4 \times 250$  mm).

**Plant Material** The fruits of *Daphniphyllum longeracemosum* were collected in Hekou of Yunnan Province, P. R. China, in October 2008. The material was identified by Prof. Xun Gong.

**Extraction and isolation** The air-dried and powdered fruits of *Daphniphyllum longeracemosum* (13.0 kg) were extracted with  $\text{CH}_3\text{OH}$ , and the crude extract was adjusted to pH 3 with 2% HCl. The acidic mixture was defatted with petroleum ether, and then subjected to cation exchange resin to give the crude alkaloid (41.0 g). The material was subjected to a silica gel CC ( $\text{CHCl}_3/\text{CH}_3\text{OH}$ , 100 : 0  $\rightarrow$  0 : 1) to obtain six major fractions (Fr.) A–F. Fr. B (2.1 g) was further chromatographed over Si gel CC (petroleum ether/ $\text{Et}_2\text{NH}$ , 100 : 1  $\rightarrow$  40 : 1, petroleum ether/ $\text{CH}_3\text{COCH}_3$ , 50 : 1  $\rightarrow$  20 : 1) followed by Sephadex LH-20 CC eluted with  $\text{CH}_3\text{OH}$  to afford compound **1** (6 mg). Fr. F (18.0 g) was separated on  $\text{C}_{18}$  silica gel, then purified by semi-HPLC ( $\text{MeOH}/\text{H}_2\text{O}$  **20** : **80**) to get **2** (68 mg), **3** (35 mg). Compounds **4** (3.2 g) was crystallized from Fr. F.

Daphlongeranine F (**1**):  $\text{C}_{24}\text{H}_{35}\text{O}_4$ , colorless solide;  $[\alpha]_{\text{D}}^{23.5} = -17.7$  ( $c = 0.15$ ,  $\text{MeOH}$ ); UV  $\lambda_{\text{max}}$  ( $\log \epsilon$ ): 296 (4.12); IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 2926, 1692, 1650, 1620 1464, 1372, 1210, 1033;  $^1\text{H}$  and  $^{13}\text{C}$  NMR data, see Table 1; Positive ESIMS  $m/z$  402  $[\text{M} + \text{H}]^+$ ; HRESIMS  $m/z$  402.2641  $[\text{M} + \text{H}]^+$  (calcd 402.2644).

Table 1 The NMR data of daphlongeranine F (**1**) in  $\text{CDCl}_3$ ,  $\delta$  in ppm,  $J$  in Hz

No.	$\delta_{\text{C}}$	$\delta_{\text{H}}$	No.	$\delta_{\text{C}}$	$\delta_{\text{H}}$
1	62.3 t	2.83 (m) 2.32 (d, 11.2)	13	42.9 t	2.61 (m) 1.88 (br. d, 14.8)
2	100.1 s	—	14	114.8 s	—
3	23.2 t	1.51 (m) 1.27 (m)	15	168.6 s	—
4	21.4 t	1.97 (m) 1.62 (m)	16	25.7 t	2.66 (m)
5	36.4 s	—	17	40.1 t	2.71 (m) 2.81 (m)
6	30.1 d	1.83 (m)	18	27.3 t	2.63 (m) 1.44 (m)
7	56.6 t	2.36 (m) 2.40 (m)	19	8.1 q	0.89 (t, 7.0)
8	46.9 s	—	20	63.1 t	4.13 (d, 12.0) 3.54 (dd, 12.0, 3.1)
9	149.3 s	—	21	167.7 s	—
10	152.4 s	—	22	46.1 q	2.13 (br. s, 3H)
11	28.5 t	2.56 (m) 1.91 (m)	2-OCH <sub>3</sub>	46.7 q	3.16 (s, 3H)
12	28.1 t	1.71 (m) 1.54 (m)	21-OCH <sub>3</sub>	51.1 q	3.68 (s, 3H)

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